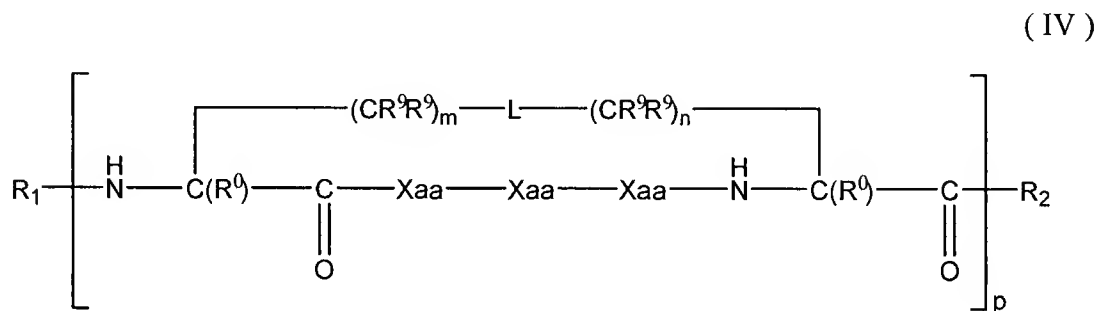


In the claims:

Please cancel claims 1-101 and add the following claims:

102. (New) A compound having a plurality of alpha helical cyclic pentapeptide sequences, which is represented by formula (IV):



wherein each Xaa is independently selected from any amino acid residue;

R₁ is selected from H, an N-terminal capping group, a peptide of 1 to 5 amino acid residues optionally capped by an N-terminal capping group, a non-peptidic group or a group that mimics an amino acid side chain;

R₂ is selected from H, a C-terminal capping group, a peptide of 1 to 5 amino acids optionally capped by a C-terminal capping group, a group that mimics an amino acid side chain or a group that activates the terminal carboxylic acid carbonyl group to nucleophilic substitution;

each R⁹ and R⁰ are independently selected from H, C₁-C₁₀alkyl, C₂-C₁₀alkenyl, C₂-C₁₀alkynyl, C₃-C₁₀cylcoalkyl, C₅-C₁₀cycloalkenyl, -OH, -OC₁-C₁₀alkyl, -NH₂, -NH(C₁-C₁₀alkyl), -N(C₁-C₁₀alkyl)₂, C₆-C₁₀aryl, C₃-C₁₀heterocyclyl, C₅-C₁₀heteroaryl and halo;

L is selected from $-\text{NH}-\text{C}(\text{O})-$, $-\text{C}(\text{O})-\text{NH}-$, $-\text{S}-\text{S}-$, $-\text{CH}(\text{OH})\text{CH}_2-$, $\text{CH}_2\text{CH}(\text{OH})-$, $-\text{CH}=\text{CH}-$, $-\text{CH}_2-\text{CH}_2-$, $-\text{NH}-\text{CH}_2-$, $-\text{CH}_2-\text{NH}-$, $-\text{CH}_2-\text{S}-$, $-\text{S}-\text{CH}_2-$, $-\text{C}(\text{O})-\text{CH}_2-$, $-\text{CH}_2-\text{C}(\text{O})-$, $-\text{S}(\text{O})_t-\text{NH}-$, $-\text{NH}-\text{S}(\text{O})_t-$, $\text{CH}_2-\text{P}(=\text{O})(\text{OH})-$ and $-\text{P}(=\text{O})(\text{OH})-\text{CH}_2-$;

m is 4,

n is 1,

t is 0, 1 or 2,

and

p is an integer from 2 to 4.

103. (New) A compound according to claim 102, wherein an individual pentapeptide sequence is a macrocycle formed by consecutively linking at least 18 to 22 atoms, wherein the first and last atoms are bonded to one another to form a ring.

104. (New) A compound according to claim 103, wherein the macrocycle is formed from 19 to 21 atoms

105. (New) A compound according to claim 103, wherein the macrocycle is formed from 20 atoms.

106. (New) A compound according to claim 102, wherein the amino-terminal and carboxy-terminal residues of an individual pentapeptide sequence are Lys and Asp, respectively.

107. (New) A compound according to claim 102, wherein the amino acid side chains of the amino-terminal and carboxy-terminal residues of an individual pentapeptide sequence are covalently linked to one another by a lactam bridge between a side chain amino group and a side chain carboxylic acid group..

108. (New) A compound according to claim 102, wherein the amino acid residues in the sequence of the peptide are selected from D- or L- α -amino acids.

109. (New) A compound according to claim 102, wherein the amino acid residues in the sequence of the peptide are selected from L- α -amino acids.

110. (New) A compound according to claim 102, wherein an individual Xaa is selected from residues that are favorable to helix formation, wherein the residues are selected

from alanine, arginine, lysine, methionine, leucine, glutamic acid, glutamine, cysteine, isoleucine, phenylalanine, tyrosine, tryptophan, histidine and aspartic acid.

111. (New) A compound according to claim 102, which comprises two consecutive alpha helical cyclic pentapeptides spaced from a third alpha helical cyclic pentapeptide by about 1, 2, 5, 8 or 9 natural or unnatural helix-forming amino acid residues.

112. (New) A compound according to claim 102, which comprises three consecutive alpha helical cyclic pentapeptides spaced from a fourth alpha helical cyclic pentapeptide by about 0, 3, 4, 6 or 7 natural or unnatural helix-forming amino acid residues.

113. (New) A compound according to claim 102, which comprises three consecutive alpha helical cyclic pentapeptides spaced from a fourth alpha helical cyclic pentapeptide by about 1, 2, 5, 6 or 9 natural or unnatural helix-forming amino acid residues.

114. (New) A compound according to claim 102, wherein individual pentapeptide sequences are different.

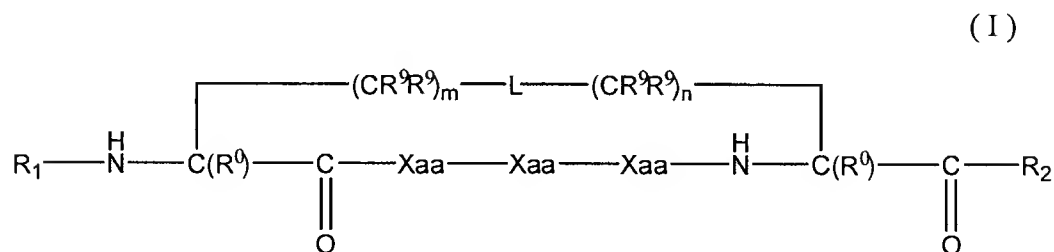
115. (New) A compound according to claim 102, wherein individual pentapeptide sequences in the peptide are the same.

116. (New) A compound according to claim 102, selected from:

cyclo(1-5, 6-10)-Ac-[KARADKARAD]-NH₂ [SEQ ID NO: 46]; and

cyclo(1-5, 6-10, 11-15)-Ac-[KARADKARADKARAD]-NH₂ [SEQ ID NO: 47].

117. (New) A compound having the formula (I):



wherein each Xaa is independently selected from any amino acid residue;

R₁ is selected from H, an N-terminal capping group, a non-peptidic group or a group that mimics an amino acid side chain;

R₂ is selected from H, a C-terminal capping group, a group that mimics an amino acid side chain or a group that activates the terminal carboxylic acid carbonyl group to nucleophilic substitution;

each R₉ and R₀ are independently selected from H, C₁-C₁₀alkyl, C₂-C₁₀alkenyl, C₂-C₁₀alkynyl, C₃-C₁₀cycloalkyl, C₅-C₁₀cycloalkenyl, -OH, -OC₁-C₁₀alkyl, -NH₂, -NH(C₁-C₁₀alkyl), -N(C₁-C₁₀alkyl)₂, C₆-C₁₂aryl, C₃-C₁₀heterocyclyl, C₅-C₁₀heteroaryl and halo;

L is selected from -NH-C(O)-, -C(O)-NH-, -S-S-, -CH(OH)CH₂-, CH₂CH(OH)-, -CH=CH-, -CH₂-CH₂-, -NH-CH₂-, -CH₂-NH-, -CH₂-S-, -S-CH₂-, -C(O)-CH₂-, -CH₂-C(O)-, -S(O)_t-NH-, -NH-S(O)_t-, CH₂-P(=O)(OH)- and -P(=O)(OH)-CH₂-;

m is 4,

n is 1, and

t is 0, 1 or 2.

118. (New) A compound according to claim 117, wherein R₁ is selected from H; an N-terminal capping group that stabilizes the terminus of a helix; a non-peptidic group; or a mimic of an amino acid side chain.

119. (New) A compound according to claim 118, wherein the N-terminal capping group is selected from acyl and N-succinate.

120. (New) A compound according to claim 118, wherein the mimic of the amino acid side chain is selected from any natural or unnatural amino acid side chain that is attached to the N-terminal amino group of the peptide through a carbonyl group derived from a carboxylic acid by formation of an amide bond.

121. (New) A compound according to claim 118, wherein the mimic of the amino acid side chain is selected from: CH₃CH₂C(O)(CH₂)_uC(O)-, NH₂(NH=)CNHC(O)(CH₂)_uC(O)-, H₂NC(O)(CH₂)₂C(O)(CH₂)_uC(O)-, HOC(O)(CH₂)₂C(O)(CH₂)_uC(O)-, HS(CH₂)₂C(O)(CH₂)_uC(O)-, H₂NC(O)(CH₂)₃C(O)(CH₂)_uC(O)-, HOC(O)(CH₂)₂C(O)(CH₂)_uC(O)-, (4-imidazolyl)(CH₂)C(O)(CH₂)_uC(O)-, CH₃CH₂CH(CH₃)CH₂C(O)(CH₂)_uC(O)-, (CH₃)₂CH(CH₂)₂C(O)(CH₂)_uC(O)-, H₂N(CH₂)₅C(O)(CH₂)_uC(O)-, CH₃S(CH₂)₃C(O)(CH₂)_uC(O)-, Ph(CH₂)₂C(O)(CH₂)_uC(O)-, Ph(CH₂)₄C(O)(CH₂)_uC(O)-, HO(CH₂)₂C(O)(CH₂)_uC(O)-,

HOCH(CH₃)CH₂C(O)(CH₂)_uC(O)-, (3-indolyl)(CH₂)₂(CH₂)_uC(O)-, (4-hydroxyphenyl)(CH₂)₂C(O)(CH₂)_uC(O)-, (4-hydroxyphenyl)(CH₂)₃C(O)(CH₂)_uC(O)-, (CH₃)₂CHCH₂C(O)(CH₂)_uC(O)-, CH₃CH₂CH₂C(O)(CH₂)_uC(O)-, C₆H₁₀CH₂C(O)(CH₂)_uC(O)-, C₅H₈CH₂C(O)(CH₂)_uC(O)-, CH₃C(O)(CH₂)_uC(O)-, CH₃(CH₂)₄C(O)(CH₂)_uC(O)-, CH₃(CH₂)₅C(O)(CH₂)_uC(O)-, HOC(O)CH₂C(O)(CH₂)_uC(O)-, HS(CH₂)C(O)(CH₂)_uC(O)-, H₂N(CH₂)₄C(O)(CH₂)_uC(O)- and HOCH₂C(O)(CH₂)_uC(O)- wherein u is 0 or an integer from 1 to 10.

122. (New) A compound according to claim 118, wherein the non-peptidic groups enhance the stability, bioavailability or activity of the peptides.

123. (New) A compound according to claim 118, wherein the non-peptidic groups is selected from: hydrophobic groups; groups which stabilize or mimic alpha-helices, groups which mimic the secondary structure of peptides; groups which improve bioavailability; and groups which are recognized by transport receptors to allow or improve transport of the peptides to the site of activity.

124. (New) A compound according to claim 117, wherein R₂ is selected from: H; a C-terminal capping group that stabilizes the terminus of a helix; a peptide of 1, 2, 3, 4 or 5 amino acid residues optionally capped with a C-terminal capping group that stabilizes the terminus of a helix; a mimic of an amino acid side chain; or a group which activates the terminal carboxylic acid carbonyl group to nucleophilic substitution.

125. (New) A compound according to claim 124, wherein the C-terminal capping group is NH₂.

126. (New) A compound according to claim 124, wherein the mimic of the amino acid side chain is any common or unnatural amino acid side chain that is attached to the C-terminal carbonyl group of the peptide through an amine group by formation of an amide bond.

127. (New) A compound according to claim 124, wherein the mimics of the amino acid side chain is selected from: -NH(CH₂)_uNHCH₂CH₃, -NH(CH₂)_uNH(CH₂)₄NHC(=NH)NH₂, -NH(CH₂)_uNH(CH₂)₂C(O)NH₂, -NH(CH₂)_uNH(CH₂)₂CO₂H, -NH(CH₂)_uNH(CH₂)₂SH, -NH(CH₂)_uNH(CH₂)₃C(O)NH₂, -NH(CH₂)_uNH(CH₂)₃CO₂H, -NH(CH₂)_uNH(CH₂)₂(4-imidazolyl), -NH(CH₂)_uNHCH₂CH(CH₃)CH₂CH₃, -NH(CH₂)_uNH(CH₂)₂CH(CH₃)₂, -

NH(CH₂)_uNH(CH₂)₅NH₂, -NH(CH₂)_uNH(CH₃)₃SCH₃, -NH(CH₂)_uNH(CH₂)₂(3-indolyl), -NH(CH₂)_uNH(CH₂)₂(4-hydroxyphenyl), -NH(CH₂)_uNH(CH₂)₃(4-hydroxyphenyl), -NH(CH₂)_uNH-CH₂CH(CH₃)₂, -NH(CH₂)_uNHCH₂CH₂CH₃, -NH(CH₂)_uNHCH₂C₆H₁₀, -NH(CH₂)_uNHCH₂C₅H₈, -NH(CH₂)_uNHCH₃, -NH(CH₂)_uNH(CH₂)₄CH₃, -NH(CH₂)_uNH(CH₂)₅CH₃, -NH(CH₂)_uNHCH₂CO₂H, -NH(CH₂)_uNHCH₂SH, -NH(CH₂)_uNH(CH₂)₂OH, -NH(CH₂)_uNH(CH₂)₅NH₂ and -NH(CH₂)_uNHCH₂OH; wherein u is 0 or an integer from 1 to 10.

128. (New) A compound according to claim 124, wherein the group, which activates the C-terminal carboxylic carbonyl group to nucleophilic substitution, converts the C-terminal carboxylic acid to a group selected from an acid chloride, an acid anhydride, an acyl azide, an O-acylisourea, a phosphonium derivative or an activated ester.

129. (New) A compound according to claim 124, wherein the non-peptidic group enhances the stability and circulating time, or decrease immunogenicity, or increase solubility, bioavailability or activity of the peptides.

130. (New) A compound according to claim 118, wherein the non-peptidic group is selected from: hydrophobic groups; groups which stabilize or mimic alpha-helices; groups which mimic the secondary structure of peptides; groups which improve bioavailability; groups that are recognized by transport receptors to allow or improve transport of the peptide(s) to the site of activity.

131. (New) A compound according to claim 117, wherein each R₉ is selected from H, CH₃, CH₂CH₃, vinyl, OH, OCH₃, NH₂, NH(CH₃), N(CH₃)₂, phenyl, F or Cl.

132. A compound according to claim 117, wherein each R₀ is selected from H, CH₃, CH₂CH₃ or vinyl.

133. (New) A compound according to claim 117, wherein each X_{aa} is any amino acid residue selected to mimic the amino acid residues in a known alpha helical peptide of interest or to prepare an unknown peptide having new properties.

134. (New) A compound according to claim 117, wherein an individual X_{aa} is the same or different as another X_{aa}.

135. (New) A compound according to claim 117, wherein an individual X_{aa} is selected from a D- or L- alpha amino acid residue.

136. (New) A compound according to claim 117, wherein the compound of formula (I) has at least one Xaa which is a D- or L- alpha amino acid residue that is favorable to helix formation.
137. (New) A compound according to claim 117, wherein 2 or 3 of Xaa are D- or L- alpha amino acid residues that are favorable to helix formation.
138. (New) A compound according to claim 137, wherein the D- or L- alpha amino acid residues are selected from alanine, arginine, lysine, methionine, leucine, glutamic acid, glutamine, cysteine, isoleucine, phenylalanine, tyrosine, tryptophan, histidine and aspartic acid.
139. (New) A compound according to claim 117, wherein L is -NH-C(O)- or -C(O)-NH- .
140. (New) A compound according to claim 117, wherein the amino-terminal and carboxy-terminal residues of the compound are Lys and Asp, respectively.
141. (New) A compound according to claim 117, selected from:
Ac-(cyclo-1,5)-[KARAD]-NH₂, [SEQ ID NO. 8];
AcR-cyclo-2,6-[KLLLD]-NH₂, [SEQ ID NO. 15];
AcR-cyclo-2,6-[KLALD]-NH₂, [SEQ ID NO. 16];
AcR-cyclo-2,6-[KLFAD]-NH₂, [SEQ ID NO. 17];
Ac-(cyclo-1,5)-[KARAD]-OH, [SEQ ID NO. 20];
H-(cyclo-1,5)-[KARAD]-NH₂, [SEQ ID NO. 21];
H-(cyclo-1,5)-[KARAD]-OH, [SEQ ID NO. 22];
Ac-(cyclo-2,6)-R[KAAAD]-NH₂, [SEQ ID NO. 23];
Ac-(cyclo-2,6)-R[KALAD]-NH₂, [SEQ ID NO. 24];
Ac-(cyclo-2,6)-R[KAMAD]-NH₂, [SEQ ID NO. 25];
Ac-(cyclo-2,6)-R[KAQAD]-NH₂, [SEQ ID NO. 26];
Ac-(cyclo-2,6)-R[KAFAD]-NH₂, [SEQ ID NO. 27];
Ac-(cyclo-2,6)-R[KAGAD]-NH₂, [SEQ ID NO. 28];
Ac-(cyclo-2,6)-R[KGSAD]-NH₂, [SEQ ID NO. 29];
Ac-(cyclo-2,6)-R[KSSSD]-NH₂, [SEQ ID NO. 30]; and
Ac-(cyclo-2,6)-R[KGGGD]-NH₂, [SEQ ID NO. 31]

142. (New) A method for constructing a constrained helical peptide, the method comprising: (1) synthesizing a peptide according to claim 102 or claim 117, wherein the peptide comprises a sequence of five amino acid residues having a first terminal residue and a second terminal residue that are separated by an intervening sequence of three amino acid residues, and wherein the individual side chains of the first and second terminal residues are linkable to each other; and (2) cyclizing the peptide by linking the side chain of the first terminal residue with the side chain of the second terminal residue, thereby yielding an alpha helical cyclic peptide.

143. (New) A method according to claim 142, wherein the first terminal residue has a side chain containing an amide bond-forming substituent and the second terminal residue has a side chain containing a functional group capable of forming an amide linkage with the side chain amide bond-forming substituent of the first terminal residue and the peptide is cyclized by reacting the side chain amide bond-forming substituent of the first terminal residue with the functional group of the second terminal residue to form an amide bond linkage, thereby yielding an alpha helical cyclic peptide.

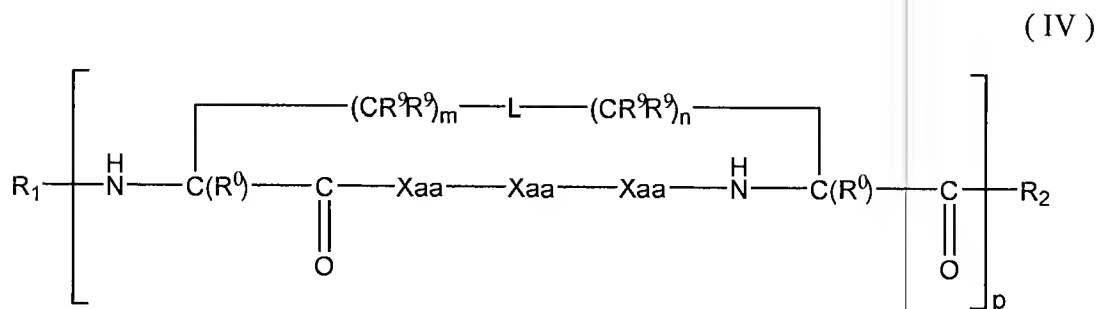
144. (New) A method according to claim 142, wherein in step (1) the reactive groups on the side chains, including the amide forming substituents, are protected by a protecting group.

145. (New) A method according to claim 142, wherein the reactive groups on the side chains, including the amide forming substituents, are deprotected prior to cyclization.

146. (New) A method according to claim 142, wherein step (2) comprises activating the carboxylic acid to nucleophilic attack by forming an acyloxyphosphonium or uronium derivative of the carboxylic acid.

147. (New) A method of producing a mimic of an alpha helical binding determinant, comprising: providing a protein of interest that comprises an alpha helical domain that interacts with a ligand; identifying a candidate binding determinant situated within a sequence of 3 or more contiguous amino acid residues in the helical binding domain; and selecting a first residue and a second residue in the sequence (designated i and $i+4$), which are separated by an intervening sequence of 3 amino acid residues, and which do not interact substantially with the ligand, for linkage to each other.

148. (New) A method according to claim 147, wherein the binding determinant is identified using mutagenesis.
149. (New) A method according to claim 147, further comprising synthesizing a peptide that comprises the first and second residues and the intervening sequence and linking the side chains of the first and second residues.
150. (New) A method according to claim 147, further comprising detecting binding of the peptide to the ligand.
151. (New) A composition comprising a compound according to claim 1 or claim 117 and a pharmaceutically acceptable carrier, diluent or adjuvant.
152. (New) A method for treating or preventing a disease or condition associated with a ligand-receptor interaction that is mediated at least in part by an alpha helical domain present in the ligand or the receptor, comprising administering an effective amount of a compound comprising at least one alpha helical cyclic peptide, wherein each peptide comprises a sequence of five amino acid residues having a first terminal residue and a second terminal residue that are separated by an intervening sequence of three amino acid residues, and wherein the side chains of the first and second terminal residues are linked to each other and wherein the side chains of at least some of the amino acid residues of the or each peptide are in a (three-dimensional) configuration that is analogous to the configuration of amino acid side chains of at least a portion of the alpha helical domain of the ligand or the receptor, wherein the compound is represented by formula (IV) or formula (I), as follows:



wherein each Xaa is independently selected from any amino acid residue;

wherein each Xaa is independently selected from any amino acid residue;

R₁ is selected from H, an N-terminal capping group, a non-peptidic group or a group that mimics an amino acid side chain;

R₂ is selected from H, a C-terminal capping group, a group that mimics an amino acid side chain or a group that activates the terminal carboxylic acid carbonyl group to nucleophilic substitution;

each R₉ and R₀ are independently selected from H, C₁-C₁₀alkyl, C₂-C₁₀alkenyl, C₂-C₁₀alkynyl, C₃-C₁₀cycloalkyl, C₅-C₁₀cycloalkenyl, -OH, -OC₁-C₁₀alkyl, -NH₂, -NH(C₁-C₁₀alkyl), -N(C₁-C₁₀alkyl)₂, C₆-C₁₂aryl, C₃-C₁₀heterocyclyl, C₅-C₁₀heteroaryl and halo;

L is selected from -NH-C(O)-, -C(O)-NH-, -S-S-, -CH(OH)CH₂-, CH₂CH(OH)-, -CH=CH-, -CH₂-CH₂-, -NH-CH₂-, -CH₂-NH-, -CH₂-S-, -S-CH₂-, -C(O)-CH₂-, -CH₂-C(O)-, -S(O)_t-NH-, -NH-S(O)_t-, CH₂-P(=O)(OH)- and -P(=O)(OH)-CH₂-;

m is 4,

n is 1, and

t is 0, 1 or 2.

153. (New) A method according to claim 152, wherein the disease or condition is related to an aberration in DNA transcription, RNA reverse transcription, transcriptional antitermination, apoptosis regulation, tumor suppression, calcium homeostasis, pain transmission, memory, lipid metabolism, cholesterol homeostasis or stress response or to anxiety, appetite, alcohol withdrawal, opiate withdrawal or epilepsy.

154. (New) A method according to claim 152, wherein the disease or condition is related to aberrant apoptosis regulation or tumor suppression.

155. (New) A method according to claim 154, wherein the compound is selected from a BH3 domain mimetic or a p53 tumor suppressor mimetic.

156. (New) A method according to claim 154, wherein the the compound is a BH3 domain mimetic selected from cyclo(2-6,7-11)-Y[KRELD][KMADD]F [SEQ ID NO: 57], cyclo(2-6,7-11)-V[KRQLD][KIADD]I [SEQ ID NO: 58], cyclo(2-6,7-11)-I[KAQED][KVADD]M [SEQ ID NO: 59], cyclo(2-6,7-11)-I[KAQED][KIADD]F [SEQ ID NO: 60], cyclo(2-6,7-11)-3-(4-hydroxyphenyl)-propionyl[KRELD][KMADD]-

phenethylamide [SEQ ID NO: 61], cyclo(2-6,7-11)-iso-valeroyl[KRQLD][KIADD]2-methylbutylamide [SEQ ID NO: 62], cyclo(2-6,7-11)-3-methylpentanoyl-[KAQED][KVADD]-3-methylsulfanyl-propylamide [SEQ ID NO: 63], cyclo(2-6,7-11)-3-methylpentanoyl-[KAQED][KIADD]-phenethylamide [SEQ ID NO: 64], Cyclo(3,7)-LR[KMADD]F [SEQ ID NO: 65], Cyclo(3,7)-LA[KIADD]I [SEQ ID NO: 66], Cyclo(3,7)-LA[KVADD]I [SEQ ID NO: 67], Cyclo(3,7)-LA[KIADD]F [SEQ ID NO: 68], Cyclo(2,6)-7-methyl octanoyl-[KMADD]-Phenethylamide [SEQ ID NO: 69], Cyclo(2,6)-7-methyl octanoyl-[KIADD]-2-methylbutylamide [SEQ ID NO: 70], Cyclo(2,6)-7-methyl octanoyl-[KVADD]-2-methylbutylamide [SEQ ID NO: 71] and Cyclo(2,6)-7-methyl octanoyl-[KMADD]-Phenethylamide [SEQ ID NO: 72].

157. (New) A method according to claim 154, wherein the p53 tumor suppressor mimetic is selected from Cyclo(3,7)-FM[K(Pmp)(6CIW)ED]L [SEQ ID NO: 73], Cyclo(3,7)-3-Phenylpropanoyl-M[K(Pmp)(6CIW)ED]isopentylamide [SEQ ID NO: 74] and Cyclo(2,6)-6-Phenylheptanoyl-[K(Pmp)(6CIW)ED]isopentylamide [SEQ ID NO: 75].

158. (New) A method according to claim 152, wherein the disease or disorder is related to pain transmission, anxiety, appetite, alcohol withdrawal, opiate withdrawal, epilepsy or memory.

159. (New) A method according to claim 158, wherein the compound is an agonist or antagonist of ORL-1 receptor.

160. (New) A method according to claim 158, wherein the compound is selected from Cyclo(6-10,11-15)-FGGFT[KARKD][KRKLD]-NH₂ (agonist) [SEQ ID NO: 76], Cyclo(6-10,11-15)-NpheGGFT[KARKD][KRKLD]-NH₂ (antagonist) [SEQ ID NO: 77], Cyclo(2-6,7-11)-Ac-T[KARKD][KRKLD]-NH₂ (antagonist) [SEQ ID NO: 78] and Cyclo(2-6,7-11)-(8-napthalen-1-yl-methyl-4-oxo-1-phenyl-1,3,8-triaza-spiro[4,5]dec-3-yl)-acetoxy-[KARKD][KRKLD]-NH₂ (antagonist) [SEQ ID NO: 79].